

Indicator: Urinary Pesticide/Herbicide Level (104)

More than one billion pounds of pesticides and herbicides are used in the United States each year to control weeds, insects, and other organisms that threaten or undermine human activities (Aspelin, 2003). Some of these compounds can be harmful to humans if ingested, inhaled, or otherwise contacted in sufficient quantities. The primary routes of exposure for the general population are ingestion of a treated food source and contact with applications in or near residential sites. Herbicide exposure may also result from contaminated water. Those who manufacture, formulate, and/or apply these chemicals may also be occupationally exposed.

This indicator reports the results of human biomonitoring for three classes of non-persistent pesticides and three classes of herbicides, which can be measured through metabolites that result from the chemical breakdown of the pesticide/herbicide within the body. Measurement of non-persistent pesticide/herbicide metabolites in urine typically reflects recent exposure (i.e., in the last few days) due to the short time these metabolites remain within the body (CDC, 2003).

The three classes of pesticides covered by this indicator are Carbamates, Organophosphates (OPs), and Pyrethroids. All three groups are neurotoxicants that act by overstimulating the nervous system of exposed organisms. Symptoms of exposure to pesticides in these classes may include muscle weakness or paralysis, difficulty breathing, difficulty concentrating, impaired coordination, and memory loss (CDC, 2003).

The three herbicide classes discussed here have all been designated by EPA as restricted use products, meaning the products are only to be used by certified applicators or under the supervision of such an applicator (EPA, 2003). The herbicide groups are: chlorophenoxy acids, triazines, and chloroacetamides. Symptoms of acute high dose exposure to these herbicides may include skin and mucosal irritation as well as burning sensations in the nasopharynx and chest if inhaled (Reigart and Roberts, 1999).

This indicator presents pesticide and herbicide urinary metabolite data collected as part of CDC's National Health and Nutrition Examination Survey (NHANES). NHANES is a series of surveys conducted by CDC's National Center for Health Statistics (NCHS) that is designed to collect data on the health and nutritional status of the civilian, non-institutionalized U.S. population using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey; biomonitoring for certain environmental chemicals also was implemented. These data are presented here as a baseline with the intent of reporting trends in the future. Carbamates, organophosphates, and herbicides were measured as part of NHANES 1999-2000; pyrethroid data were collected in NHANES 2001-2002. This indicator presents data for a subsample of survey participants ages 6 to 59 years; the sample size for each chemical was between 1,800 and 2,000 individuals. NHANES also measured levels of a class of persistent pesticides, the organochlorine pesticides, which are not discussed here but can be found under the Indicator "Blood POPs Level" (POPs = Persistent Organic Pollutants).

What the Data Show

Carbamates. Table 104-1 Carbamate presents the geometric means for unadjusted and creatinine-adjusted urinary concentrations of the carbamate pesticide metabolites. Of the three metabolites presented, only 1-naphthol was detected with sufficient frequency to calculate a measurable geometric mean which was 1.70 µg/L and 1.52 µg/g (creatinine-adjusted).

Organophosphates. NHANES 1999-2000 measured urinary concentrations of dialkyl phosphates, which are the primary metabolites of many organophosphate compounds. Table 104-2 Organophosphate presents the geometric means for urinary concentrations and creatinine-adjusted urinary concentrations of these metabolites. Only two of the six urinary dialkyl phosphates presented (dimethylthiophosphate and

diethylphosphate) were measured with sufficient frequency above the limit of detection to calculate a geometric mean. The geometric means for those metabolites were 1.82 µg/L (1.64 µg/g creatinine) and 1.03 µg/L (0.92 µg/g creatinine), respectively.

Pyrethroids. *This is a placeholder for the data that will be released as part of the Third National Report on Human Exposure to Environmental Chemicals from CDC. Pyrethroids were collected in NHANES 2001-2002. Release of this report is pending, but should be out before release ROE06.*

Herbicides. None of the direct metabolites of the three primary classes of herbicide were detected in urine with sufficient frequency above the limit of detection to calculate a geometric mean. The metabolites 2,4,5-trichlorophenoxyacetic acid and atrazine mercapturate were detected in only 1.2% and 3.3%, respectively, of the subsample (CDC, 2003). The minor metabolite 2,4-dichlorophenol had a geometric mean of 1.1 µg/L measured in urine; however, this metabolite can also be a result of metabolism of several other chemicals or a byproduct in the manufacture of chemicals.

Indicator Limitations

- NHANES selects a representative sample of the civilian, non-institutionalized population in the United States using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey. With only 2 years of data in NHANES 1999-2000, instead of the 6-years for NHANES III (1988-1994), some differences exist that may limit the underlying data with respect to completeness or representative of coverage.
 - The sample size is smaller and the number of geographic units in the sample is more limited. The current 1999-2000 NHANES survey is nationally representative but it is subject to the limits of increased sampling error due to (1) the smaller number of individuals sampled in the annual sample and (2) the smaller number of Primary Sampling Units (PSUs) [see description below] available for each annual sample. Therefore, the sample size for any 1-year period is relatively small, possibly resulting in large variability for U.S. population estimates, especially those for narrowly defined demographic groups or other specific subgroup analyses.
 - For NHANES 1999-2000, the first stage of selection was the primary sampling unit (PSU) level. PSUs were defined as single counties. For a few PSUs, the county population was too small and those counties were combined with geographically contiguous counties to form a PSU. The 1999-2000 NHANES sample is selected from a relatively small number of PSUs compared to NHANES III. With a small number of PSUs, variance estimates that account for the complex design may be relatively unstable, a factor which introduces a higher level of uncertainty in the annual estimates.
 - NHANES is designed to increase precision by combining data across calendar years. Because of the relatively small sample size in 1999 and 2000, analytical data for just one or two survey participants may be weighted heavily and greatly influence the mean value reported.
 - The number of geographic sites sampled each year is small and environmental exposures may vary geographically; thus producing environmental exposure estimates by geographic region using the NHANES data set is of limited value.
- The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical has caused or will cause harmful effects.
- Generally recognized guidelines for urinary levels of carbamate, organophosphate, herbicide, and pyrethroid metabolites have not yet been established.
- Some metabolites may result from sources other than pesticide exposure. For example, 1-naphthol in the urine may reflect multiple sources of exposure, and is therefore not just an indicator of carbamate pesticide exposure.

Data Sources

Centers for Disease Control and Prevention. 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004)

<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

Centers for Disease Control and Prevention. *Results from NHANES 2001-2002 (anticipated release prior to publication of ROE'06)*

References

Aspelin AL. 2003. Pesticide Usage in the United States: Trends During the 20th Century. Raleigh, NC: Center for Integrated Pest Management, North Carolina State University. February 2003.

http://www.pestmanagement.info/pesticide_history/index.pdf.

Centers for Disease Control and Prevention. 2003. Second National Report on Human Exposure to Environmental Chemicals. (Accessed November 21, 2004)

<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

Environmental Protection Agency. 2003. Restricted Use Products (RUP) Report. (Accessed March 10, 2005) <http://www.epa.gov/opprd001/rup/>

Reigart JR, Roberts JR. Recognition and Management of Pesticide Poisonings. (1999) Prepared for U.S. Environmental Protection Agency (Accessed April 11, 2005)

<http://www.epa.gov/pesticides/safety/healthcare/handbook/contents.htm>

Graphics

Table 104-1 Carbamate. Geometric mean and selected percentiles for unadjusted and creatinine-adjusted urinary concentrations of selected carbamate metabolites among a subsample of participants aged 6-59 years from National Health and Nutrition Examination Survey (NHANES), 1999-2000

	Sample Size	Geometric Mean	10 th	25 th	50 th	75 th	90 th
1-Naphthol							
µg/L of urine	1998	1.70	<LOD	<LOD	1.22	2.72	6.20
µg/g of creatinine*	1998	1.52	<LOD	<LOD	1.25	3.00	6.80
2-Isopropoxyphenol							
µg/L of urine	1917	NC	<LOD	<LOD	<LOD	<LOD	<LOD
µg/g of creatinine*	1917	NC	<LOD	<LOD	<LOD	<LOD	<LOD
Carbofuranphenol							
µg/L of urine	1994	NC	<LOD	<LOD	<LOD	<LOD	<LOD
µg/g of creatinine*	1994	NC	<LOD	<LOD	<LOD	<LOD	<LOD

* µg per gram of creatinine in urine

<LOD= Less than the limit of detection of the analytical method.

NC= Not calculated – Proportion of results below limit of detection was too high to provide a valid result.

Source: Centers for Disease Control and Prevention. Second National Report on Human Exposure to Environmental Chemicals. January 2003. (Accessed November 21, 2004)

<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

Table 104-2 Organophosphate. Geometric mean and selected percentiles for unadjusted and creatinine-adjusted urinary concentrations of selected organophosphate metabolites for the United States population, aged 6-59 years, National Health and Nutrition Examination Survey (NHANES), 1999-2000

	Sample Size	Geometric Mean	10 th	25 th	50 th	75 th	90 th
Dimethylphosphate							
µg/L of urine	1949	NC	<LOD	<LOD	0.74	2.80	7.90
µg/g of creatinine*	1949	NC	<LOD	<LOD	0.81	2.93	8.46
Dimethylthiophosphate							
µg/L of urine	1948	1.82	<LOD	<LOD	2.70	10.0	38.0
µg/g of creatinine*	1948	1.64	<LOD	<LOD	2.12	9.57	32.0
Dimethyldithiophosphate							
µg/L of urine	1949	NC	<LOD	<LOD	<LOD	2.30	12.0
µg/g of creatinine*	1949	NC	<LOD	<LOD	<LOD	1.86	10.1
Diethylphosphate							
µg/L of urine	1949	1.03	<LOD	<LOD	1.20	3.10	7.50
µg/g of creatinine*	1949	0.92	<LOD	<LOD	0.93	2.73	7.94
Diethylthiophosphate							
µg/L of urine	1949	NC	<LOD	<LOD	0.49	0.76	1.3
µg/g of creatinine*	1949	NC	<LOD	<LOD	0.25	0.71	1.7
Diethyldithiophosphate							
µg/L of urine	1949	NC	<LOD	<LOD	0.08	0.20	0.47
µg/g of creatinine*	1949	NC	<LOD	<LOD	0.07	0.20	0.55

* µg per gram of creatinine in urine

<LOD= Less than the limit of detection of the analytical method.

NC= Not calculated – Proportion of results below limit of detection was too high to provide a valid result.

Source: Centers for Disease Control and Prevention. Second National Report on Human Exposure to Environmental Chemicals. January 2003 (Accessed November 21, 2004)

<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

R.O.E. Indicator QA/QC

Data Set Name: URINARY PESTICIDE/HERBICIDE LEVEL

Indicator Number: 104 (89119)

Data Set Source: CDC, NHANES

Data Collection Date: ongoing

Data Collection Frequency: 2 year cycle

Data Set Description: Urinary Pesticide/Herbicide level Note: Pesticides that are considered Persistent Organic Pollutants (POPs) will be found in the POPs section.

Primary ROE Question: What are the trends in biomeasures of exposure to common environmental pollutants including across population subgroups and geographic regions?

Question/Response

T1Q1 Are the physical, chemical, or biological measurements upon which this indicator is based widely accepted as scientifically and technically valid?

Yes. Urine samples were collected and processed in accordance with the methods indicated in the NHANES Specimen Collection and Laboratory/Medical Technologists Procedures Manual (LPM). See: <http://www.cdc.gov/nchs/data/nhanes/blood.pdf>
<http://www.cdc.gov/nchs/data/nhanes/LAB1-6.pdf> See
<http://www.cdc.gov/nchs/data/nhanes/frequency/l26ppdoc.pdf> for the description of laboratory procedures for pesticide measurement.

T1Q2 Is the sampling design and/or monitoring plan used to collect the data over time and space based on sound scientific principles?

Yes. NHANES is designed to provide statistically representative national averages. Starting with NHANES 1999, the survey is conducted annually. A subsample of participants aged 6-59 years in NHANES 1999-2000 were measured for urine levels of the pesticide metabolites. Subsamples were randomly selected within the specified age range to be a representative sample of the U.S. population. The measurements produced by NHANES for this indicator were used in the Second National Report on Human Exposure to Environmental Chemicals published by the National Center for Environmental Health in 2003.
<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

T1Q3 Is the conceptual model used to transform these measurements into an indicator widely accepted as a scientifically sound representation of the phenomenon it indicates?

Not applicable

T2Q1 To what extent is the indicator sampling design and monitoring plan appropriate for answering the relevant question in the ROE?

This indicator is based on a national probability-based sampling design and is deemed of sufficient quality for generalization to the nation. The samples for 1999-2000 were used for this analysis. Quality assurance measures were in place. Beginning in 1999, NHANES became a continuous and annual survey. The sampling plan for each year follows a complex, stratified, multistage, probability-cluster design to select a representative sample of the civilian, noninstitutionalized population. Every year, approximately 7,000 individuals, of all ages, are interviewed in their homes; of these, approximately 5,000 complete the health examination

component of the survey. The survey sample size for NHANES 1999-2000 is 9,965 (<http://www.cdc.gov/nchs/data/nhanes/gendoc.pdf>).

T2Q2 To what extent does the sampling design represent sensitive populations or ecosystems?

The current sampling design includes oversampling of African Americans, Mexican Americans, adolescents (12-19 year olds), older Americans (60 years of age and older), and pregnant women to produce more reliable estimates for these groups.

T2Q3 Are there established reference points, thresholds or ranges of values for this indicator that unambiguously reflect the state of the environment?

This indicator simply provides information that exposure to a pesticide has occurred. Generally recognized guidelines for urinary levels of these pesticide metabolites have not been established. Measurements of urinary pesticide metabolites provide an estimate of exposure to various classes of pesticides; however, without additional information, linking these metabolites to specific pesticides is not possible. Furthermore, finding a measurable amount of one or more metabolites in urine does not by itself mean that the chemical has caused or will cause harmful effects. More research is needed to identify at which levels urinary pesticide metabolites constitute a health concern. As reported in Second National Report on Human Exposure to Environmental Chemicals published by the National Center for Environmental Health in 2003.

<http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf>

T3Q1 What documentation clearly and completely describes the underlying sampling and analytical procedures used?

Documentation for NHANES 1999-2000 is found on NCHS/CDC website at the following URL: http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm#Laboratory%20Files The following provides more specific examples: The Addendum to the NHANES III for the 1999-2000 dataset clearly outlines the 1999-2000 sampling design and recommends analytic procedures. <http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>

<http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf> The Second National Report on Human Exposure to Environmental Chemicals published by the National Center for Environmental Health in 2003 more generally describes the NHANES 1999-2000 sampling plan. <http://www.cdc.gov/exposurereport/2nd/pdf/secondner.pdf> The NHANES 1999-2000 subsampling webpage clearly describes the subsampling methods used and how subsampled data should be analyzed <http://www.cdc.gov/nchs/about/major/nhanes/subsample.htm> as do the Weighting Notes posted on the NHANES website

<http://www.cdc.gov/nchs/data/nhanes/frequency/weights%20to%20usev6.pdf>

T3Q2 Is the complete data set accessible, including metadata, data-dictionaries and embedded definitions or are there confidentiality issues that may limit accessibility to the complete data set?

For the most part, Individual level data are available, but data access limitations do exist for some variables due to confidentiality issues.

http://www.cdc.gov/nchs/about/major/nhanes/nhanes99_00.htm#Laboratory%20Files

T3Q3 Are the descriptions of the study or survey design clear, complete and sufficient to enable the study or survey to be reproduced?

Yes. The Addendum to the NHANES III for the 1999-2000 dataset clearly outlines the 1999-2000 sampling design and recommends analytic procedures.

<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>
<http://www.cdc.gov/nchs/data/nhanes/nhanes3/nh3gui.pdf>

T3Q4 To what extent are the procedures for quality assurance and quality control of the data documented and accessible?

The quality assurance plans for NHANES 1999-2000 are available from the Division of Data Dissemination, NCHS, 6525 Belcrest Rd. Hyattsville, MD, 20782-2003. Tel. 301-458-4636. Internet: <http://www.cdc.gov/nchs/about/quality.htm>

T4Q1 Have appropriate statistical methods been used to generalize or portray data beyond the time or spatial locations where measurements were made (e.g., statistical survey inference, no generalization is possible)?

Yes. The NHANES 1999-2004 survey is designed to be annually nationally representative of the U.S. citizen, non-institutionalized population. (see page 11 of the addendum linked below)
<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>

T4Q2 Are uncertainty measurements or estimates available for the indicator and/or the underlying data set?

Yes. (see pages 11-19 of the addendum linked below)
<http://www.cdc.gov/nchs/data/nhanes/guidelines1.pdf>

T4Q3 Do the uncertainty and variability impact the conclusions that can be inferred from the data and the utility of the indicator?

NHANES selects a representative sample of the civilian, non-institutionalized population in the United States using a complex, stratified, multistage, probability-cluster design. Beginning in 1999, NHANES became a continuous and annual national survey. With only 2 years of data in NHANES 1999-2000, instead of the 6-years for NHANES III (1988-1994), some differences exist that may limit the underlying data with respect to completeness or representative of coverage. The sample size is smaller and the number of geographic units in the sample is more limited. The current 1999-2000 NHANES survey is nationally representative but it is subject to the limits of increased sampling error due to (1) the smaller number of individuals sampled in the annual sample and (2) the smaller number of Primary Sampling Units (PSUs) [see description below] available for each annual sample. Therefore, the sample size for any 1-year period is relatively small, possibly resulting in large variability for U.S. population estimates, especially those for narrowly defined demographic groups or other specific subgroup analyses. For NHANES 1999-2000, the first stage of selection was the PSU-level. The PSUs were defined as single counties. For a few PSUs, the county population was too small and those counties were combined with geographically contiguous counties to form a PSU. The 1999-2000 NHANES sample is selected from a relatively small number of PSUs compared to NHANES III. With a small number of PSUs, variance estimates that account for the complex design may be relatively unstable, a factor which introduces a higher level of uncertainty in the annual estimates. NHANES is designed to increase precision by combining data across calendar years. Because of the relatively small sample size in 1999 and 2000, analytical data for just one or two survey participants may be weighted heavily and greatly influence the mean value reported. The number of geographic sites sampled each year is small and environmental exposures may vary geographically; thus producing environmental exposure estimates by geographic region using the NHANES data set is of limited value.

<http://www.cdc.gov/nchs/about/major/nhanes/subsample.htm>

T4Q4 Are there limitations, or gaps in the data that may mislead a user about fundamental trends in the indicator over space or time period for which data are available?

As subsequent years are added to this survey, estimates will become more stable. However, with the laboratory data, there is no guarantee that an environmental chemical will be measured from year to year. The measurement of an environmental chemical in a person's blood or urine does not by itself mean that the chemical has caused or will cause harmful effects.